REMARKS

Claims 1-38, 42, 43, 58, 59, 73, 79, 82, 89-91, 99 and 113-140 were pending in this application with claims 1, 38, 42, 43, 59, 73, 79, 82, 89, 90, 91 and 99 being independent claims. Claims 9, 42, 43 and 116-122 have been amended. New claims 141-203 have been added. Therefore, claims 1-38, 42, 43, 58, 59, 73, 79, 82, 89-91, 99 and 113-203 are now pending. Support for the claim amendments and new claims can be found throughout the specification and in the claims as filed. No new matter has been added.

Information Disclosure Statement

The Examiner has indicated that copies of the items listed in the Information Disclosure Statement filed on August 28, 2002 are not with the file. Although Applicant has previously provided copies of the items listed in the Information Disclosure Statement to the USPTO, Applicant is herewith providing new copies of the items listed for the Examiner's consideration. Also provided is a new PTO Form 1449 for the Examiner to initial and include with the next communication to the Applicant.

Claim Objections

The Examiner has objected to claims 38, 42 and 58 as being substantial duplicates of claim 1. Applicant respectfully traverses the Examiner's objection of the claims on this basis.

Applicant maintains that claims 38, 42 and 58 each are of different scope than that of claim 1. Claim 1 is a method wherein an effective amount of an unformulated dry polysaccharide particle is administered to a pulmonary tissue. Claim 38, however, is directed to patentably distinct subject matter as the claim is directed to a method of delivering an unformulated dry polysaccharide particle, wherein at least 5% of the polysaccharide is administered and is delivered to the lower respiratory tract. This is obviously distinct from claim 1 as the at least 5% of the polysaccharide of claim 38 is not necessarily the same as the therapeutically effective amount of claim 1. Furthermore, the at least 5% of the polysaccharide of claim 38 is for administration to the lower respiratory tract, while claim 1 does not contain this limitation. Therefore, although the claims have overlapping scope, the breadth of the claims are not identical nor substantial duplicates.

With regard to claim 42, the claim is directed to the systemic delivery of the polysaccharide, which is different than claim 1 and claim 38 which embrace both systemic or local delivery. Although not necessary, Applicant has amended claim 42 to incorporate this limitation into the body of the claim to clarify the distinction of this claim.

Finally, claim 58 is directed to administering to a pulmonary tissue a composition of unformulated dry glycosaminoglycan rather than the polysaccharides as specified in the other claims. Claim 58, therefore, is of narrower scope than that of the other claims in that the method pertains to administering a glycosaminoglycan versus any polysaccharide.

Based on the arguments presented above, Applicant maintains that the claims are not the same and respectfully request the Examiner withdraw his objection of the claims.

Rejections Under 35 U.S.C. §112

Claims 1-37, 42, 58, 59, 73, 79, 82, 89-91, 99 and 116-140 are rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner has rejected the claims for various reasons which are described further below.

Effective Amount

The Examiner states that the term "effective amount" of claim 1 is indefinite as "the claim fails to state the function which is to be rendered effective". Applicant respectfully disagrees. The claim clearly provides that the effective amount (of the polysaccharide) is one which produces a therapeutic effect. This clearly indicates the function for the effective amount of the polysaccharide. In addition, this term is well-recognized such that one of ordinary skill in the art would understand what an effective amount of the claims for a particular therapeutic purpose would be. Furthermore, this term is sufficiently defined in the specification on, for example, pages 25 and 26. It, therefore, is not indefinite and would be clear to one of ordinary skill in the art.

Unformulated Polysaccharide, Glycosaminoglycan, Heparin

The Examiner has also rejected all claims that contain the terms "unformulated" or "formulated" as, according to the Examiner, it is unclear as to what is intended by these terms. As also described elsewhere herein, Applicant's invention is based in part on the important discovery that successful intrapulmonary delivery of polysaccharides (e.g., glycosaminoglycans, heparin) can be accomplished using unformulated polysaccharides. The meaning of unformulated polysaccharide particles or preparations would be apparent to one of ordinary skill in the art and is provided in the specification, for example, on page 12, lines 24-30. From this definition it is clear that the unformulated polysaccharide particles or preparations are those that do not include carriers or other excipients that enhance delivery or result in slow release, although they may include agents that are not expected to influence the

polysaccharide's delivery or absorption. Furthermore, the term "formulated particles" is defined on page 15, lines 17-32. This definition provides that formulated particles are those that include at least one carrier or excipient. In addition, examples of surfactants (a type of excipient) as well as other controlled release materials are given on pages 15-16. Such definitions are adequate to define the terms unformulated and formulated so that they are sufficiently clear and not indefinite.

Low Molecular Weight Heparin

The Examiner has rejected all of the claims that use the term "low molecular weight heparin" (LMWH), such as in claim 5, as, according to the Examiner, one of ordinary skill in the art would not be reasonably apprised of the scope of the claims. Applicant respectfully disagrees and maintains that further defining low molecular weight heparin in the claims is not necessary. Low molecular weight heparin refers to the shorter chains that are present in a standard heparin composition defined on page 21, lines 15 and 16 of the specification. The definition provides that LMWH preparations are heparin preparations that generally have a molecular weight of about 3,000 to about 8,000 Daltons. Examples of LMWH preparations are also provided thereafter in the specification through the first 3 lines on page 16. Furthermore, low molecular weight heparin is a well-recognized term of art. Over 5,000 references (to date) in the PubMed database use this term. A quick review of these references indicates that the term dates back to as early as 1972. Such an art-recognized term cannot be deemed indefinite as the Examiner asserts.

Biotechnology Derived Heparin

The Examiner indicates that it is unclear how the method of claim 6 will be affected by reciting that the heparin is a "biotechnology-derived heparin". It is the Examiner's contention that it is unclear how the recitation of the source of the agent further limits the method. Applicant respectfully disagrees with the Examiner's assessment. Applicant maintains that dependent claim 6 narrows the scope of the method in that the method is directed to administering an unformulated dry biotechnologically derived heparin particle rather than a heparin from some other source. The method is, therefore, further limited in that the agent for administration is different and more narrow than that of the previous claim (claim 5), which is directed to the administration of any low molecular weight heparin obtained from biotechnological techniques or from a natural source.

Chemically Modified Heparin

The Examiner has rejected the claims for the recitation of "modified heparin", as, according to the Examiner, the identity of a "modified heparin" would be difficult to ascertain. Applicant maintains that "modified heparin" is not difficult to ascertain and is, therefore, not indefinite. As the Examiner has pointed out, heparin is an art known compound. Applicant asserts that one of ordinary skill in the art is able to not only recognize heparin but also the heparins that have been modified based on the knowledge of the art-recognized compound and the plain meaning of modified (or changed). If one of ordinary skill in the art is able to recognize heparin itself it follows that one of ordinary skill is able to recognize those heparins that have been changed. Finally, Applicant respectfully reminds the Examiner that Applicant is not claiming the modified heparins themselves but merely the method of using them. One of ordinary skill in the art, therefore, need only recognize whether or not a particular heparin molecule has been modified or changed to know whether or not practicing the method with that molecule is encompassed by the claims.

Oligosaccharide

The Examiner has rejected claim 9 as it is unclear how the claim can be further limited from polysaccharide to oligosaccharide. Applicant has amended claim 9 to clarify that the oligosaccharide is one that binds AT-III. The amendment is believed to be sufficient to overcome the Examiner's rejection.

Unfractionated Heparin Preparation

The Examiner has rejected the claims for the use of the term "unfractionated heparin preparation". This again is a well-recognized term that is used to refer to preparations of heparin that have not undergone fractionation and, therefore, contain heparins of variable length (shorter and longer heparin chains). Additionally, the term can be regarded as a term of art as it has been used in over 1800 references (to date) in the PubMed database.

Derivative

The Examiner has rejected claim 32 for the recitation of "pectin derivative", as, according to the Examiner, the identity of the moieties intended to modify a pectin would be difficult to ascertain. Applicant respectfully traverses the rejection. Again, Applicant points out that the claim is not directed to the pectin derivatives themselves but merely a method of using them. One of ordinary skill in the art is familiar with what derivatives of compounds are. Therefore, one of ordinary skill in the art would be able to recognize a pectin derivative and, therefore, recognize the class of molecules for use in the claimed

method. Furthermore, although chemical derivatives are widely known in the art, the specification provides examples of such derivatives on page 16, lines 29-31. The examples given include, for example, substitutions, additions of chemical groups, for example, alkyl, alkylene, hydroxylations, oxidations, etc all known to those of skill in the relevant art.

Composition

The Examiner has rejected claim 43 for being indefinite as a composition must contain two things and for using closed language. Although the Applicant respectfully disagrees with the Examiner's rejection of the claims, Applicant has amended claim 43 as well as claims 116-122 which depend therefrom in order to expedite the prosecution of this application.

Rapidly or Rapid

The Examiner has rejected claims 59, 73 and 79 for the use of "rapid" or "rapidly", which, according to the Examiner, are relative terms not defined by the claim. Applicant respectfully disagrees. Applicant maintains that even if, *arguendo*, the terms were indefinite, which Applicant does not agree that they are, the claims clearly define the requisite timeframe that the terms in the preamble refer to. Therefore, the claims are not indefinite.

Heparin-like Glycosaminoglycan

The Examiner has rejected claims 82, 89 and 90 for the use of "heparin-like glycosaminoglycans" as being a relative term which renders the claims indefinite. Applicant respectfully disagrees. This term is defined in the specification on page 20, lines 28-30 as a family of molecules having heparin-like structures and properties. One of ordinary skill in the art is familiar with the structure of heparin as well as its properties. Additionally, extensive examples of molecules that fall within this family are provided on page 20, lines 30-32. Based on the definitions provided as well as the knowledge of those of ordinary skill in the art, one of ordinary skill in the art would recognize the molecules encompassed by the rejected claims.

Detection System

The Examiner has rejected claim 91 for being indefinite as the Examiner maintains that it is unclear what a detection system is and for what reason it is included in the claim. Applicant respectfully traverses this rejection. The Examiner is respectfully reminded that the claims must be read in light of the specification. Detection systems are adequately defined (and examples provided), for example, on page

33, lines 16-30 of the specification. The specification also provides that the detection system may be useful where the administration of the polysaccharide is dependent on the level of the polysaccharide in the blood. Additionally, other uses for a detection system of the kits of the claim will be apparent to one of ordinary skill in the art. Based on the above arguments and due to the fact that one of ordinary skill in the art will recognize what detection systems are and what they can be used for, the claim as written is not indefinite.

Rejections Under 35 U.S.C. §102

The Examiner has rejected claims 43 and 118 under 35 U.S.C. §102(b) as being anticipated by Platz et al. (WO96/32149). The Examiner maintains that Platz et al. anticipates the claims because Platz et al. teaches a heparin composition with particles having a diameter of 3.5 microns (Example IX), while our claims are drawn to a composition of unformulated dry glycosaminoglycan with a mean geometric diameter of 1-500 microns (claim 43) or 1-5 microns (claim 118).

Applicant respectfully traverses the rejection of claims 43 and 118 on this basis. An important distinction between the teachings of Platz et al. and the rejected claims is that claims 43 and 118 are drawn to unformulated dry glycosaminoglycan. The heparin compositions of Platz et al., however, are not unformulated dry heparin compositions. While Applicant's provide that their glycosaminoglycan compositions do not contain a carrier or excipient that affect delivery or result in slow release, the heparin compositions of Platz et al. are not unformulated.

Accordingly, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §103

The Examiner rejected claims1-38, 42, 43, 58, 59, 73, 79, 82, 89, 90 and 113-140 under 35 U.S.C. §103(a) as being unpatentable over Sackner et al. (4,679,555) in view of Edwards et al. (WO98/31346) and Platz et al. (WO96/32148).

Similar to the arguments presented above, claims 1-38, 42, 43, 58 and 113-129 are directed to compositions and methods of using unformulated dry polysaccharides (glycosaminoglycans). None of the references cited by the Examiner either alone or in combination teach unformulated dry polysaccharides as provided by the Applicants.

Additionally, Applicant maintains that the references cited by the Examiner either alone or in combination do not provide all of the limitations of the rejected claims. Claim 59, for instance, provides a method of delivering a dry aerosol containing a polysaccharide to a pulmonary tissue in an amount such that a peak plasma concentration of polysaccharide is produced within two hours. None of Sackner et al.,

Edwards et al. or Platz et al. teach or suggest such a method. One of ordinary skill in the art would not know how to go about performing the method or that such a method could be performed without the teachings provided by Applicant. In regard to claim 73 and its dependent claims 130-134, a method is provided that requires that the dry aerosol containing a polysaccharide is delivered in an amount such that at least 5% of the polysaccharide is delivered to the blood within one hour. Neither of these limitations are provided by any of the references cited by the Examiner. Similarly, claim 79 provides a method to deliver a dry aerosol containing a polysaccharide in an amount to produce a therapeutic effect in one hour. The amount or timeframe to produce the therapeutic effect are also not taught or suggested by these references.

Finally, claims 82, and its dependent claims (claims 135-140), 89 and 90, limit the heparin-like glycosaminoglycan particles to size parameters not provided by Sackner et al., Edwards et al. or Platz et al. Claim 82 limits the mean geometric diameter of the particles to greater than 30 microns. None of the references teach particles with a mean geometric diameter greater than 30 microns. Although on page 8, lines 18-21, and page 17, line 32, through page 18, lines 1-3, Edwards et al. vaguely alludes to particles with larger diameters, there is no specific teaching of particles with a mean geometric diameter greater than 30 microns. Furthermore, Edwards et al. actually teaches away from using such large particles in the passage on page 8 by pointing out that larger particles are not phagocytosed as are the desired particles of their invention. The particles of the invention of Edwards et al. are clearly taught to have a mean geometric diameter of between 5 and 30 microns. Claim 89 restricts the particle size encompassed by the scope of the claim to particles with a mean aerodynamic diameter greater than 5 microns. None of the references suggest such a size limitation. In fact, Edwards et al. specifically provides that the particles of their invention have a mean aerodynamic diameter that is between 1 and 5 microns, and preferably between 1 and 3 microns. Finally, claim 90 provides particles with a tap density of greater than 0.4 g/cm^3. Again, none of the references provides a specific teaching of a dry aerosol formulation of particles with a tap density greater than 0.4 g/cm^3 containing a heparin-like glycosaminoglycan. Furthermore, although Edwards et al. teaches estradiol-containing particles with a tap density of 0.46 g/cm^3 and 0.62 g/cm^3, these particles are estradiol-containing and not heparin-like glycosaminoglycan-containing as provided in claim 90. Further, this teaching was merely an illustration of the preparation of large porous particles. No motivation is provided in these references that would lead one of ordinary skill in the art to combine this teaching in Edwards et al. with that of the other references to obtain the heparin-like glycosaminoglycan particles of Applicant's claim. In fact, the other teachings provided by Edwards et al. teaches away from making particles with greater tap density as the focus of the Edwards et al. reference is to make aerodynamically light particles. Such particles are taught to have a tap density of less than 0.4

g/cm^3. In order for a *prima facie* case of obviousness, there must be a motivation to combine the references to produce all of the limitations of the claim. These limitations are not provided by the combination of the references cited against the Applicant.

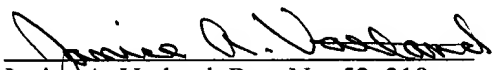
Accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's representative at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
Liu et al., Applicant

By: 

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